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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,587	11/21/2003	Takuya Watanabe	55862CIP(46342)	5293

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EXAMINER	
ULM, JOHN D	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 04/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,587	WATANABE ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-82* is/are pending in the application.

4a) Of the above claim(s) *8-15,17,19,28-34,36,60,61,65-69 and 79-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,20,59,62-64,70-75,77,78 and 2145* is/are rejected.

7)☒ Claim(s) *16,18,22-27,35,37-44 and 76* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/21/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 1 to 82 are pending in the instant application.

2) Claims 16, 18, 22 to 27, 35, 37 to 44 and 76 stand objected to under 37 CFR 1.75(c) as being in improper form for those reasons of record in the previous office action. See MPEP § 608.01(n). Accordingly, the claims 16, 18, 22, to 27, 35, 37 to 44, 70 and 76 have not been further treated on the merits.

3) Claims 2, 46 and 62 are objected to as reciting an improper Markush Group. M.P.E.P. 803.02 states that:

> "Since the decisions in In re Weber **,198 USPQ 328 (CCPA 1978); and In re Haas, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention, In re Harnish , 631 F.2d 716, 206 USPQ 300 (CCPA 1980); Ex Parte Hozumi , 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

The multiple sequences recited in these claims do not reflect a common inventive concept because they lack a common utility that is based upon a common structural feature or combination of features that distinguishes them as a group from, the prior are. For example, the only common feature of the peptides recited in sections 2 and 3 of claim 62 is the RF amide motif that was well known in the prior art, as disclosed on page 2 of the instant specification.

4) Claims 8 to 15, 17, 19, 28 to 34, 36, 60, 61, 65 to 69 and 79 to 82, as well as claims 1 to 7, 20, 21, 45 to 59, 62 to 64, 70 to 75, 77 and 78 in so far as they relate to an amino acid sequence other than SEQ ID NO:1 or 8, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the

restriction (election) requirement in the reply filed on 09 February of 2006. The traversal is on the grounds that "the inventions are not independent" and "[b]ecause the amino acid [sequence] represented by SEQ ID NO:1 includes amino acid sequences represented by SEQ ID NO: 8, SEQ ID NO: 14, SEQ ID NO: 18, SEQ ID NO: 33 and SEQ ID NO: 50, there is some degree of overlap in the searches for Groups I to VI.. This is not found persuasive because, whereas SEQ ID NO:1 is contained in its entirety within SEQ ID NO:8, SEQ ID NO:1 is not contained within SEQ ID NOs: 14, 18, 33 or 50 nor is the sequence presented in any one of SEQ ID NOs: 14, 18, 33 or 50 contained within SEQ ID NO:1 or SEQ ID NO:8. Therefore, in the absence of an admission on the record that each of these sequences is obvious over any one of the others, a search for more than one of these sequences in a single application constitutes an undue burden.

Applicant's request that "[I]f the Examiner is aware of another method to make the product as claimed, using a process which is materially different from that set forth in the restricted claims, applicant respectfully requests the Examiner to substantiate his position in greater detail" is acknowledged. Applicant is advised that a polypeptide of the instant invention can be produced by conventional peptide synthesis as described on page 174 of the instant specification or isolated from a natural source as described on page 184 therein, since the disclosed polypeptides occur in nature. Applicant is further advised that substantially more complex proteins such as insulin, papain and trypsin had been purified decades before DNA technology was developed.

Further, M.P.E.P. 803 states that:

" For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant."

In addition, a traversal is on the ground(s) that a restriction requirement is only proper when inventions are "independent and distinct" is not persuasive because this premise is completely in conflict with current patent practice as explained in M.P.E.P. 803 as follows.

803 Restriction - When Proper [R - 2]

Under the statute an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04(j)) or distinct>(< MPEP § 806.05 - § 806.05(I)).

If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to distinct or independent inventions.

CRITERIA FOR RESTRICTION BETWEEN PATENTABLY DISTINCT INVENTIONS

There are two criteria for a proper requirement for restriction between patentably distinct inventions:

(1) The inventions must be independent (see MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (see MPEP § 806.05 - § 806.05(I)); and

(2) There must be a serious burden on the examiner if restriction is not required (see MPEP § 803.02 § 806.04(a) - (j), § 808.01(a) and § 808.02).

GUIDELINES

Examiners must provide reasons and/or examples to support conclusions, but need not cite documents to support the requirement in most cases.

Where plural inventions are capable of being viewed as related in two ways, both applicable criteria for distinctness must be demonstrated to support a restriction requirement.

If there is an express admission that the claimed inventions are obvious over each other within the meaning of 35 U.S.C. 103, restriction should not be required, In re Lee, 199 USPQ 108 (Deputy Asst. Comm'r. for Pats 1978).

For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows **by** appropriate explanation either **separate classification**, separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant. Insofar as the criteria for restriction practice relating to Markush - type claims is concerned, the criteria is set forth in MPEP § 803.02. Insofar as the criteria for restriction or election practice relating to claims to genus - species, see MPEP § 806.04(a) - (j) and MPEP § 808.01(a).

Because Applicant's traversal is based upon a premise which is directly contrary to current patent practice as explained above and an initial search burden was shown by separate classification of the different inventions the requirement is still deemed proper and is therefore made FINAL.

5) The drawings in the instant application do not comply with 37 C.F.R. § 1.821(d), which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. M.P.E.P. 2422.02 expressly states that "when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings".

6) The instant specification does not comply with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. Specifically, the text in line 9 on page 185 and in lines 26 to 28 on page 189 of the instant specification describes amino acid sequences without employing the required sequence identifier. Correction is required. See M.P.E.P. 2422.03.

7) Claims 3 to 7 and 47 to 57 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The test as to whether a claim is a proper dependent claim is that it shall include every limitation of the claim from which it depends (35 U.S.C. 112, fourth paragraph) or in other words that it shall not conceivably be infringed by anything which would not also infringe the basic claim. Claim 3 can be infringed by a polypeptide consisting only of the amino acid sequence presented in residues 81 to 92 of SEQ ID NO:1. Such a polypeptide would not infringe claim 1, which requires the entire amino acid sequence presented in SEQ ID NO:1. Therefore, claim 3 can not properly depend from claim 1 because claim 3 can conceivably be infringed by something which would not also infringe claim 1. See 608.01(n)III. Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8) Claims 3, 7, 20, 21, 47, 52 to 59, 77 and 78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. These claims encompass subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In so far as the instant claims encompass a "partial peptide" of SEQ ID NO:1 or 8 comprising anything other that residues 81 to 92, 101 to 112 or 124 to 131 of SEQ ID NO:1, the instant specification provides absolutely no reasonable expectation that any other portion of SEQ ID NO:1 has any biological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that:

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Because there is no evidence or sound scientific reasoning provided by the instant specification to support a conclusion that all or a specific portion of the amino acid sequence of SEQ ID NO:1, other than those three portions containing the art recognized RF amide motif, will stimulate prolactin secretion in a mammal, an artisan

can not "predict by resort to known scientific law" that a particular "partial peptide" will have the required activity.

9) Claims 45 to 53, 55 to 59, 72, 77 and 78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. These claims encompass subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In so far as these encompass "a prolactin secretion regulatory agent" having other than stimulatory activity, no such agent is described in the instant specification. There is absolutely no evidence of record that supports an assertion that one of the RF amide peptides described in the instant specification has inhibitory activity at any concentration. The theory that increasing concentrations of a receptor agonist will desensitize a receptor in not consistent with an inhibitory role for that agonist because desensitization and inhibition are not the samne process nor do they produce the same result. For example, it is well known in the art that adrenaline is an agonist for the adrenergic receptors and yet administering increasing levels of adrenaline in a mammal certainly does not produce a decrease in the heart rate or blood pressure of that mammal, except when death results.

In so far as these claims encompass an agent for the prevention or treatment of a specific disorder, the instant specification fails to disclose the details of any specific method of treating other than those provided by Example 14 therein, which did not treat or prevent any particular disease or disorder. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed

into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and produce a medicament for use in the recited method without first making a substantial inventive contribution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10) Claims 1 to 7, 20, 21, 45 to 59, 73 to 75 and 77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10.1) Claims 1 to 7, 20 and 21 are vague and indefinite because the metes and bounds of the limitation "substantially the same" is undeterminable when employed to define a structural element in a chemical compound. The term "substantially the same" is vague because it is not possible to determine at what point in deviation a different but

similar sequence would cease to be "substantially the same" as the reference sequence.

10.2) Claim 7 is vague and indefinite because there is no antecedent basis for "the partial peptide".

10.3) Claims 73 to 75 and 77 provide for the use of a peptide, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11) Claims 73 to 75 and 77 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

12) Claims 1 to 7, 20, 21, 45 to 59, 62 to 64 and 70 to 72 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims encompass a polypeptide as it occurs in nature.

13) Claims 1, 2, 20, 21, 45, 46, 52, 54 to 59, 77 and 78 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed

specific and substantial credible utility and because they are drawn to an invention that is inoperative in its current form. These claims encompass a polypeptide comprising the entire amino acid sequence presented in SEQ ID NO:1 of the instant application. The instant application has provided a description of an isolated DNA encoding a preproprotein comprising four putative RF-amide-like polypeptides, and the preproprotein encoded thereby. Whereas Example 14 of the instant specification shows that the exogenous administration of a peptide consisting of residues 81 to 93 from the amino acid sequence presented in SEQ ID NO:1 of the instant specification stimulated the production of prolactin when administered to rats, there is absolutely no evidence that a protein comprising the entire amino acid sequence presented in SEQ ID NO:1 has any useful biological activity at all. One of ordinary skill in the art of molecular biology would reasonably conclude, from the evidence of record, that the amino acid sequences presented in SEQ ID NO:1 and 8 of the instant application correspond to the amino acid sequence of a naturally occurring biologically inactive precursor protein that is processed by the cell producing it into at least the four active peptides disclosed in the specification as being contained therein. Whereas a protein of the instant invention may serve as a precursor protein in its native environment, a purified form of that protein lacks a specific and substantial utility in currently available form because the instant specification does not disclose even a single procedure that would result in the conversion of that protein into one or more of the active peptides described in the instant specification. It is noted that those peptides of the instant invention that have

been shown to be biologically active in the instant specification were not derived from a precursor protein comprising all of SEQ ID NO:1 or 8.

Because a peptide comprising SEQ ID NO:1 of the instant application has no demonstrable biological activity and the instant application fails to disclose a process of administering that peptide in a manner that results in it being processed into one or more active reagents that peptide has no specific utility as a clinical reagent. Further, because neither the instant specification nor the art of record provides the guidance needed to employ the claimed peptide as a substrate in a process of producing a biologically active reagent, Applicant has left it to the practitioner of the art to make those additional inventive contributions needed to use the claimed peptide in a practical application.

14) Claims 1, 2, 20, 21, 45, 46, 52, 54 to 59, 77 and 78 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is inoperable in currently available form for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

15) The prior art of record did not disclose or suggest an isolated peptide comprising residues 81 to 92, 101 to 112 or 124 to 131 of SEQ ID NO:1 of the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
PRIMARY EXAMINER
GROUP 1800